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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,710	04/19/2007	Margaret Dunkley	ADAM-41138	8808

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
07/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,710	DUNKLEY, MARGARET	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 33-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/06; 5/07; 2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 4-22-09 has been entered into the record.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statements filed 5-30-07 and 2-20-09 have been considered.

The information disclosure statement filed 8-17-06 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because no copies of the references have been provided. It has been placed in the application file, but the information referred to therein has not been considered as to the merits.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Election/Restrictions

Applicant's election with traverse of Group 2, claims 17-32 in the response filed 4-22-09 is acknowledged. The traversal is on the ground(s) that Pasquale et al does destroy unity of invention. This is not found persuasive because the formulation of the art anticipates claim 1 and as applicants admit, the intranasal immunization provides for lung delivery of the polyvalent soluble antigen of the art and as such meets the limitation of formulated for the lungs.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-16 and 33-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 4-22-09.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 19, 22, 24-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kyd et al (Infection and Immunity, 63(8):2931-2940, 1995; of record on 1449).

Kyd et al teach a prime (peyer's patch) boost (intratracheal) method of vaccination providing for enhanced respiratory clearance of nontypeable *H. influenzae* (NTHi). Rats were immunized with by peyers's patch immunization with emulsification of the purified 200 ug of outer membrane P6 protein in incomplete Freund's adjuvant. Rats receiving an intratracheal boost were immunized 10 ug of outer membrane P6 protein in phosphate buffered saline. The purified outer membrane P6 is a purified cellular fraction, soluble containing more than one epitope/valency and was isolated by known procedures involving a crude outer membrane preparation and subsequent isolation (see page 2932, column 1, purification of P6). Kyd et al teach that the pulmonary boost with P6 enhanced the protective capacity of the antigen-specific response such that the clearance with observed after challenges with both capsule and acapsular NTHi strains. Kyd et al teach that essential for successful induction of clearance of HTHi challenge was the ability to induce effective mucosal antigen specific responses *in vivo* leading to the recruitment of phagocytic cells to the lungs (see page 2939, column 2, last paragraph). As such the claims are anticipated.

Claims 17, 19, 22, 24, 25, 26, 27, 28, 29 and 30 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Eyles et al (Vaccine 18:3266-3271, 2000; of record on 1449).

Eyles et al teaches the administration and protection from *Yersinia pestis* infection by administration of purified *Yersinia pestis* F1 and V subunits via the bronchopulmonary route. The recombinant soluble F1 and V subunits were isolated from cellular matter are in fact a cellular fraction and were administered together in the presence and in the absence of microsphere formulations. The microsphere formulations were protective from infection.

Claims 17-19, 22-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Latil et al (Journal of Clinical Microbiology, 23(6):1015-1021, 1986).

Latil et al teach the administration of a lysed multivalent aerosol vaccine to human subjects (see abstract). The vaccine comprised lysed bacteria from *S. penumoniae*, *N. catarrhalis*, *N. flavia*, *K. penumoniae*, *M. pyogenes* and *H. influenzae*. The lysed pacteria pereparateion was in distilled water and filtered twice through a membrane of 0.20 uM pore size to yield a clear solution. The patients received 5 mls aerosol doses of the bacterial solution (see page 1016, column 1, see Vaccine and Immunization). Latil et al teach that the immunization provided for IgA production (See page 1018, Figure 2) for *S. pneumoniae* Types II and II and Streptococcus sp. Inasmuch as, the claims require the generation of an immune response, the method and composition of Latil et al anticipate the instantly claimed invention. Additionally, there is no apparent difference in a lysate versus a sonicate because both break open the cells and in the absence of evidence to the contrary the lysate anticipates the sonicate because they have antigens in common and both contain polyvalent soluble antigen and cellular matter.

Claims 17-19, 22-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Johansen et al (APMIS 100:87-90, 1992; of record).

Johansen et al teach the administration of a sonicated *Pseudomonas aeruginosa* 579 vaccine as a sonicated soluble extract and viable bacteria were removed by filtration (0.22

uM) and the protein concentration of the antigen preparation was 12.8g/L. Rats were immunized intratrachealy with the vaccine in 0.1 ml of a preparation diluted to 2.0 mg/ml of sonicated antigen. Intratracheal immunization provides for local IgA production and systemic IgG production (see page 89, columns 1-2). In view of the local and systemic immune responses, the mammals are inherently protected and/or treated.

Claims 17-19, 22-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Johansen et al (APMIS 99:1061-1068, 1991; of record).

Johansen et al teach the administration of a sonicated Pseudomonas aeruginosa 579 vaccine as a sonicated soluble extract and viable bacteria were removed by filtration (0.22 uM) and the protein concentration of the antigen preparation was 12.8g/L (page 1062, columns 1-2). Rats were immunized intratrachealy with the vaccine in 0.1 ml of a preprateion diluted to 2.0 mg/ml of sonicated antigen. Intratracheal immunization provides for local IgA production and systemic IgG production (see page 1065, columns 1-2). Johansen et al teach that no illness was observed with the animal treated with the sonicate (see page 1064 paragraph bridging columns 1-2). In view of the local and systemic immune responses, the mammals are inherently protected and/or treated.

Claims 17 and 20-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kyd et al (Infection and Immunity, 63(8):2931-2940, 1995) in view of Kreig et al (US Patent 7,524,828, with priority to October 30, 1997).

Kyd et al teach a prime (peyer's patch) boost (intratracheal) method of vaccination providing for enhanced respiratory clearance of nontypeable *H. influenzae* (NTHi). Rats were immunized with by peyers's patch immunization with emulsification of the purified 200 ug of outer membrane P6 protein in incomplete Freund's adjuvant. Rats receiving an intratracheal boost were immunized 10 ug of outer membrane P6 protein in phosphate buffered saline. The purified outer membrane P6 is a purified cellular fraction, soluble

containing more than one epitope/valency and was isolated by known procedures involving sonication to form a crude outer membrane preparation and subsequent isolation (see page 2932, column 1, purification of P6). Kyd et al teach that the pulmonary boost with P6 enhanced the protective capacity of the antigen-specific response such that the clearance with observed after challenges with both capsule and acapsular NTHi strains. Kyd et al teach that essential for successful induction of clearance of HTHi challenge was the ability to induce effective mucosal antigen specific responses *in vivo* leading to the recruitment of phagocytic cells to the lungs (see page 2939, column 2, last paragraph).

Kreig et al teach CpG adjuvants useful for the treatment of viral, bacteria, fungal or parasitic infection (see paragraph bridging columns 6-7) to stimulate a subject's response to a vaccine. Kreig et al teach that the CpG adjuvants stimulate a Th1 pattern of immune activation, cytokine production, NK lytic activity and B cell proliferation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to add to the soluble sonicate of Kyd et al the CpG adjuvant of Kreig et al and administer the adjuvated vaccine composition intratrachealy for the boost because Kreig et al teach that the CpG adjuvants are useful for stimulating a subjects response to a vaccine and thereby useful for the treatment of bacterial infections.

Claims 17, 18, 19, 22 and 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kyd et al (Infection and Immunity, 63(8):2931-2940, 1995; hereinafter Kyd (1); of record) in view of Kyd et al, Vaccine, 14(15):1471-1478, 1996; hereinafter Kyd (2)) and Kyd et al (Infection and Immunity, 62(12):5652-5658, 1994; hereinafter Kyd(3)).

Kyd et al teach a prime (peyer's patch) boost (intratracheal) method of vaccination providing for enhanced respiratory clearance of nontypeable *H. influenzae* (NTHi). Rats were immunized with by peyers's patch immunization with emulsification of the purified 200 ug of outer membrane P6 protein in incomplete Freund's adjuvant. Rats receiving an

intratracheal boost were immunized 10 ug of outer membrane P6 protein in phosphate buffered saline. The purified outer membrane P6 is a purified cellular fraction, soluble containing more than one epitope/valency and was isolated by known procedures involving to form a crude outer membrane preparation comprising multiple outer-membrane proteins including P2 and subsequent isolation (see page 2932, column 1, purification of P6). Kyd et al teach that the pulmonary boost with P6 enhanced the protective capacity of the antigen-specific response such that the clearance with observed after challenges with both capsule and acapsular NTHi strains. Kyd et al teach that essential for successful induction of clearance of NTHi challenge was the ability to induce effective mucosal antigen specific responses *in vivo* leading to the recruitment of phagocytic cells to the lungs (see page 2939, column 2, last paragraph). Kyd et al differ by not administering the outer membrane protective protein P6 or P6 containing other cellular matter.

Kyd (2) teaches that outermembrane P2 isolated according to Kyd et al above provides for enhanced clearance of bacteria from the lungs following pulmonary challenge (see page 1475, discussion bridging columns 1-2). Significant levels of P2-specific IgG, IgA and IgM were measured in both serum and bronchial lavage fluids (page 1475, column 2, second paragraph).

Kyd (3) teaches the crude outer-membrane extract comprising both P6 and P2 from NTHi (see OMP extraction page 5653, column 1). Kyd (3) teaches that that crude outer-membrane extract was able to stimulate T-cells from immunized individuals (page 5657, Figure 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to substitute the crude outer-membrane extract of Kyd(3) for the purified outer-membrane P6 extract in the method of immunizing of Kyd(1) because Kyd (3) teaches a fraction containing both protective P6 and P2 outer-membrane antigens. The combination of protective antigens in a crude extract would be expected to function equivalently or better in the protection by means of enhanced clearance of bacteria.

Furthermore, the use of a crude extract comprising protective outer-membrane antigens would provide the advantages of less processing time and would make the vaccines cheaper to produce.

Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kyd et al (Infection and Immunity, 63(8):2931-2940, 1995; hereinafter Kyd (1); of record), Kyd et al, Vaccine, 14(15):1471-1478, 1996; hereinafter Kyd (2)) and Kyd et al (Infection and Immunity, 62(12):5652-5658, 1994; hereinafter Kyd(3)) as applied to claims 17, 18, 19, 20-22 and 24-32 and further in view of Kreig et al (US Patent 7,524,828, with priority to October 30, 1997).

Kyd(1), Kyd(2) and Kyd(3) are set forth supra. The combination differs by not teaching the use of adjuvants in the intratracheal immunization.

Kreig et al teach CpG adjuvants useful for the treatment of viral, bacteria, fungal or parasitic infection (see paragraph bridging columns 6-7) to stimulate a subject's response to a vaccine. Kreig et al teach that the CpG adjuvants stimulate a Th1 pattern of immune activation, cytokine production, NK lytic activity and B cell proliferation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to add to the crude outer-membrane vaccine as combined surpa the CpG adjuvant of Kreig et al and administer the adjuvated vaccine composition intratrachealy for the boost because Kreig et al teach that the CpG adjuvants are useful for stimulating a subjects response to a vaccine and thereby useful for the treatment of bacterial infections.

Claims 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kyd et al (Infection and Immunity, 63(8):2931-2940, 1995; hereinafter Kyd (1); of record), Kyd et al, Vaccine, 14(15):1471-1478, 1996; hereinafter Kyd (2)) and Kyd et al (Infection and Immunity, 62(12):5652-5658, 1994; hereinafter Kyd(3)) as applied to claims 17, 18, 19, 20-

22 and 24-32 and further in view Granoff et al (US Patent 6,936,261, with priority to at least July 27, 2001).

Kyd(1), Kyd(2) and Kyd(3) are set forth supra. The combination differs by not teaching the use of sonication as a means to obtain the outermembrane fraction for immunization.

Granoff et al teach that convention use of lysing cells to obtain outer membrane vesicles including lysing the cells by the addition of detergent, ostmotic shock, sonciation, cavitation, homogenization or the like) (see column 14, liens 18-35). Granoff et al teach that the outer membrane fraction can be further purified.

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to substitute sonication for detergent extraction in the method of making the outer membrane preparation according to Kyd(1-3) as combined supra and use the cell sonicate in place of the detergent preparation because Kyd (3) teaches that detergents have differential effects on the ability to stimulate T cells.

Claims 17, 18 and 20-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansen et al (APMIS 99:1061-1068, 1991; of record) in view of Kreig et al (US Patent 7,524,828, with priority to October 30, 1997).

Johansen et al teach the administration of a sonicated Pseudomonas aeruginosa 579 vaccine as a sonicated soluble extract and viable bacteria were removed by filtration (0.22 uM) and the protein concentration of the antigen preparation was 12.8g/L (page 1062, columns 1-2). Rats were immunized intratrachealy with the vaccine in 0.1 ml of a preprateion diluted to 2.0 mg/ml of sonicated antigen. Intratracheal immunization provides for local IgA production and systemic IgG production (see page 1065, columns 1-2). Johansen et al teach that no illness was observed upon challenge with the animal treated with the sonicate (see page 1064 paragraph bridging columns 1-2). Johansen et al differ by not administering the sonicate in the presence of an adjuvant.

Kreig et al teach CpG adjuvants useful for the treatment of viral, bacteria, fungal or parasitic infection (see paragraph bridging columns 6-7) to stimulate a subject's response to a vaccine. Kreig et al teach that the CpG adjuvants stimulate a Th1 pattern of immune activation, cytokine production, NK lytic activity and B cell proliferation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to add to the soluble sonicate of Johansen the CpG adjuvant of Kreig et al and administer the adjuvated vaccine composition because Kreig et al teach that the CpG adjuvants are useful for stimulating a subjects response to a vaccine and thereby useful for the treatment of bacterial infections.

Status of the Claims

Claims 17-32 stand rejected. Claims 1-16 and 33-47 are withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Primary Examiner